

AMENDMENT

Please cancel and re-write Claim 8 as new Claim 115 as follows:

115. (New) The method of Claim 1, wherein said compound is an a MSH analog selected from the group consisting of:

a. Ac-[Cys⁴, D-Phe⁷, Cys¹⁰] α -MSH, wherein said Cys residues are connected by a disulfide bond;

b. Ac-[Nle⁴, X_{aa}⁵, His⁶, X_{aa}⁷, Arg⁸, Trp⁹, X_{aa}¹⁰] NH₂, (SEQ ID NO:3) wherein X_{aa}⁵ is Glu or Asp, X_{aa}⁷ is Phe or D-Phe and X_{aa}¹⁰ is a dibasic amino acid; Lys; ornithine; 2,4,-diaminobutyric acid; or 2,3 diaminopropionic acid (Dpr);

c. Ac-[Cys⁴, Cys¹⁰] α -MSH₁₋₁₃NH₂;

d. R₁-W-X-Y-Z-R₂,
wherein R₁ is selected from the group consisting of Ac-Gly-, Ac-Met-Glu-, Ac-Nle-Glu- and Ac-Tyr-Glu-;
W is selected from the group consisting of -His- and -D-His-;
X is selected from the group consisting of -Phe-, -D-Phe-, -Tyr, -D-Tyr-, (-pNO₂)D-Phe⁷;
Y is selected from the group consisting of -Arg- and -D-Arg-;
Z is selected from the group consisting of -Trp- and -D-Trp-; and,
R₂ is selected from the group consisting of -NH₂, -Gly-NH₂, and -Gly-Lys-NH₂;

e. Ac-Ser-Tyr-Ser-M-Glu-His-D-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH₂ (SEQ ID NO:4),
wherein M is selected from the group consisting of Met, Nle, and Cys;

f. [Nle⁴, D-Phe⁷]- α -MSH;

g. [Nle⁴, D-Phe⁷] - α -MSH₄₋₁₀;

h. [Nle⁴, D-Phe⁷] - α -MSH₄₋₁₁;

i. [Nle⁴, D-Phe⁷,D-Trp⁹] - α -MSH₄₋₁₁;

j. [Nle⁴, D-Phe⁷] - α -MSH₄₋₉; and

k. Ac-[Nle⁴, AA⁵, D-Phe⁷, AA¹⁰]-R₁ or Ac-[Nle⁴, AA⁵, D-Phe⁷, AA¹¹]-R₂;

wherein AA⁵ may be either a L- or D-amino acid having an omega amino or carboxyl group in the side chain;

wherein AA¹⁰ may be diaminopropionic acid, α,γ -diaminobutyric acid, Orn, Lys, α,β -amino adipic acid, α -aminopimelic acid, or higher homologs, Glu or Asp;

wherein R₁ is the designation α -MSH₁₋₁₃NH₂, α -MSH₁₋₁₂NH₂, α -MSH₁₋₁₁H₂; α -MSH₄₋₁₃NH₂, or α -MSH₄₋₁₀NH₂;

wherein AA¹¹ may be L- or D-amino acid having an omega amino or carboxyl group in the side chain;

wherein R₂ is the designation α -MSH₁₋₁₃NH₂, α -MSH₁₋₁₂NH₂, α -MSH₁₋₁₁NH₂, α -MSH₄₋₁₃NH₂, or α -MSH₄₋₁₀NH₂;

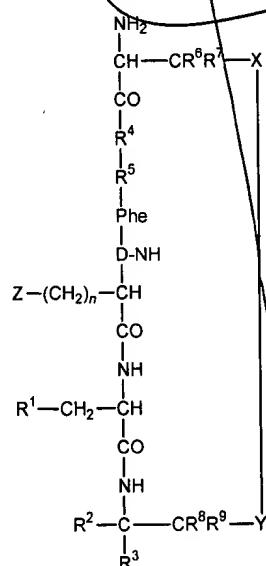
l.

Ac-Nle-Asp-His-D-Nal-Arg-Trp-Lys-NH₂; and (SEQ ID NO:5)

m.

Ac-Nle-Asp-His-D-p-I-Arg-Trp-Lys-NH₂; and (SEQ ID NO:6); and,

n.



wherein R¹ is a substituted or unsubstituted aromatic radical;

R² is hydrogen or a methyl group;

*R*³ is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;
*R*⁴ is glutamic acid, alanine, -amino butyric acid, valine, leucine or isoleucine;

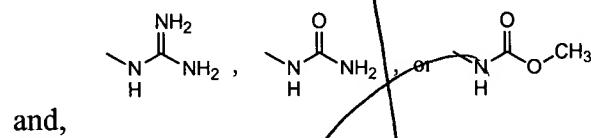
*R*⁵ is histidine, glutamic acid, alanine, valine, leucine or isoleucine;

*R*⁶ and *R*⁷, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

*R*⁸ and *R*⁹, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

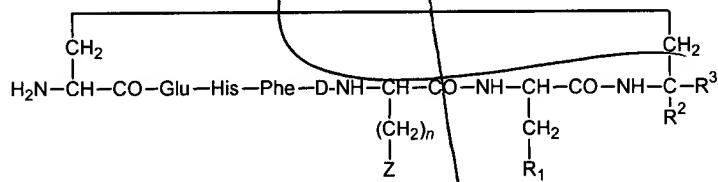
X and *Y* are sulfur, methylene, SO or SO₂;

Z is -NH₂,



n is an integer greater than or equal to 2;

o.



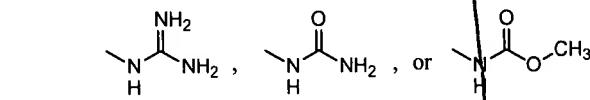
wherein *R*¹ is phenyl, indole, p-hydroxyphenyl, p-aminophenyl, imidazole, 1-naphthyl adamantly or alkylphenyl, 2-naphthyl;

*R*² is hyrdrogen or a methyl group;

*R*³ is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

X and *Y* are sulfur, methylene, SO or SO₂;

Z is -NH₂,



and,

n is an integer greater than or equal to 2; and wherein the cyclized portion of the compound is conformationally restricted in a manner which is compatible with the reactivity of the compound with receptors of the central nervous system.

[Please cancel and re-write Claim 74 as new Claim 116 as follows:]

116. (New) The therapeutic composition of Claim 68, wherein said POMC compound is an α -MSH analog selected from the group consisting of:

a. Ac-[Cys⁴, D-Phe⁷, Cys¹⁰] α -MSH, wherein said Cys residues are connected by a disulfide bond;

b. Ac-[Nle⁴, X_{aa}⁵, His⁶, X_{aa}⁷, Arg⁸, Trp⁹, X_{aa}¹⁰] NH₂, (SEQ ID NO:3) wherein X_{aa}⁵ is Glu or Asp, X_{aa}⁷ is Phe or D-Phe and X_{aa}¹⁰ is a dibasic amino acid; Lys; ornithine; 2,4,-diaminobutyric acid; or 2,3 diaminopropionic acid (Dpr);

c. Ac-[Cys⁴, Cys¹⁰] α -MSH₁₋₁₃NH₂;

d. R₁-W-X-Y-Z-R₂,
wherein R₁ is selected from the group consisting of Ac-Gly-, Ac-Met-Glu-, Ac-Nle-Glu- and Ac-Tyr-Glu-;
W is selected from the group consisting of -His- and -D-His-;
X is selected from the group consisting of -Phe-, -D-Phe-, -Tyr, -D-Tyr-, (-pNO₂)D-Phe⁷-;
Y is selected from the group consisting of -Arg- and -D-Arg-;
Z is selected from the group consisting of -Trp- and -D-Trp-; and,
R₂ is selected from the group consisting of -NH₂, -Gly-NH₂, and -Gly-Lys-NH₂;

e. Ac-Ser-Tyr-Ser-M-Glu-His-D-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH₂ (SEQ ID NO:4),
wherein M is selected from the group consisting of Met, Nle, and Cys;

f. [Nle⁴, D-Phe⁷]- α -MSH;

g. [Nle⁴, D-Phe⁷] - α -MSH₄₋₁₀;

h. [Nle⁴, D-Phe⁷] - α -MSH₄₋₁₁;

i. [Nle⁴, D-Phe⁷,D-Trp⁹] - α -MSH₄₋₁₁;

j. [Nle⁴, D-Phe⁷] - α -MSH₄₋₉; and

k. Ac-[Nle⁴, AA⁵, D-Phe⁷, AA¹⁰]-R₁ or Ac-[Nle⁴, AA⁵, D-Phe⁷, AA¹¹]-R₂;
wherein AA⁵ may be either a L- or D-amino acid having an omega amino or carboxyl group in the side chain;

wherein AA¹⁰ may be diaminopropionic acid, α,γ -diaminobutyric acid, Orn, Lys, α,β -amino adipic acid, α -aminopimelic acid, or higher homologs, Glu or Asp; wherein R₁ is the designation α -MSH₁₋₁₃NH₂, α -MSH₁₋₁₂NH₂, α -MSH₁₋₁₁H₂; α -MSH₄₋₁₃NH₂, or α -MSH₄₋₁₀NH₂;

wherein AA¹¹ may be L- or D-amino acid having an omega amino or carboxyl group in the side chain;

wherein R₂ is the designation a MSH₁₋₁₃NH₂, α -MSH₁₋₁₂NH₂, α -MSH₁₋₁₁NH₂, α -MSH₄₋₁₃NH₂, or α -MSH₄₋₁₀NH₂;

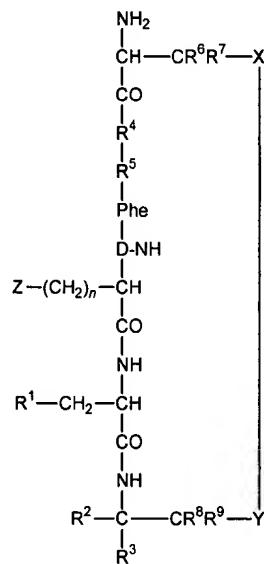
l.

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Ac—Nle—Asp—His—D—Nal—Arg—Trp—Lys—NH₂ ; and (SEQ ID NO:5)

contd.
m.

Ac—Nle—Asp—His—D—p—I—Arg—Trp—Lys—NH₂ ; and (SEQ ID NO:6); and,

n.



wherein R¹ is a substituted or unsubstituted aromatic radical;

R² is hydrogen or a methyl group;

R³ is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

*R*⁴ is glutamic acid, alanine, -amino butyric acid, valine, leucine or isoleucine;

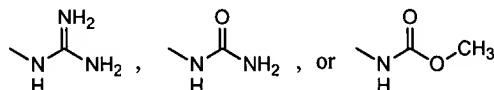
*R*⁵ is histidine, glutamic acid, alanine, valine, leucine or isoleucine;

*R*⁶ and *R*⁷, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

*R*⁸ and *R*⁹, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

X and *Y* are sulfur, methylene, SO or SO₂;

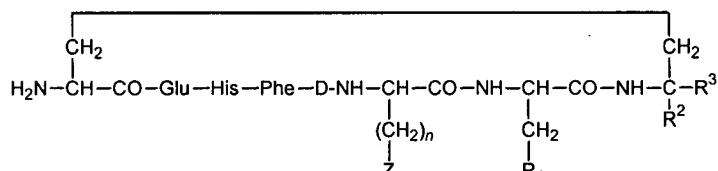
Z is -NH₂,



and,

n is an integer greater than or equal to 2;

o.



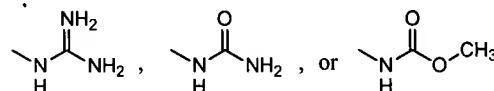
wherein *R*¹ is phenyl, indole, p-hydroxyphenyl, p-aminophenyl, imidazole, 1-naphthyl adamantly or alkylphenyl, 2-naphthyl;

*R*² is hydrgoen or a methyl group;

*R*³ is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

X and *Y* are sulfur, methylene, SO or SO₂;

Z is -NH₂,



and,

n is an integer greater than or equal to 2; and wherein the cyclized portion of the compound is conformationally restricted in a manner which is compatible with the reactivity of the compound with receptors of the central nervous system.

Please add the following new claims:

117. (New) The method of claim 115, wherein (k) AA⁵ is α,γ -diaminopropionic acid, α,γ -diaminobutyric acid, Orn, Lys, α,β -amino adipic acid, α -aminopimelic acid, or higher homologs, Glu or Asp and AA¹¹ is α,β -diaminopropionic acid, α,γ -diaminobutyric acid, Orn, Lys, α -amino adipic acid, α -aminopimelic acid, Glu or Asp.

118. (New) The therapeutic composition of claim 116, wherein (k) AA⁵ is α,γ -diaminopropionic acid, α,γ -diaminobutyric acid, Orn, Lys, α,β -amino adipic acid, α -aminopimelic acid, or higher homologs, Glu or Asp and AA¹¹ is α,β -diaminopropionic acid, α,γ -diaminobutyric acid, Orn, Lys, α -amino adipic acid, α -aminopimelic acid, Glu or Asp.

REMARKS REGARDING AMENDMENTS

Applicants thank the examiner for the opportunity to discuss the restriction and the invention on May 22, 2002. Applicants reiterate the election below.

Claims 1, 4-7, 9, 10, 13, 16, 18-21, 23-29, 31-39, 53-57, 59, 66-68, 70, 73, 75, 80-82, 85-91, 93-95, 98-100, 102, 103 and 108-118 are pending.

Applicants request amendments to the claims to clarify the invention and move the prosecution forward. Both Claim 8 and Claim 74 have been canceled and rewritten as new Claims 115 and 116 respectively, in part due to the square brackets present in the claims. The use of these brackets is based on standard peptide nomenclature, as employed by those in the art. It is hoped that by canceling these claims and replacing them with new claims we will avoid confusion regarding what has been amended in the claim, since under 37 U.S.C. § 1.121 specifies that changes be shown by brackets. In sub-section (b) of new Claims 115 and 116 the numbering of the Arg amino acid has been changed from 7 to 8. The use of 7 is clearly a typographical error since there cannot be two amino acids at position 7 of the peptide. In addition the Ac- group in Claim 115(a) and 116(a) was moved to the outside of the bracket, indicating that the N-terminus, and not the cysteine, is acetylated. Again, this will correct a typographical error since the claim specifies that the cysteine residues are connected by a disulfide bond, which would be impossible if either of the cysteines were acetylated. Next Claims 115 and 116 were broken into dependant claims 117 and 118 respectively. Finally the reference to an "Xxx" amino acid in Claim 8(k) and 74(k) has been